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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,099	07/31/2006	Paul Gregor	2819.002	4261

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,099	GREGOR ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 28-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-35 are pending.

2. Applicant's election without traverse of Group III, claims 19-27 directed to a method for inhibiting cell adhesion or cell migration comprising the step of exposing a cell to a small organic compound which interacts with at least one GAG in an amount sufficient for preventing the interactions of the GAG with at least one GAG specific ECAM, wherein HS-GAG and L-selectin are the species, filed on 9/12/08, is acknowledged.

3. Claims 1-18 and 28-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

4. Claims 19-27 are under examination as they read on to a method for inhibiting cell adhesion or cell migration comprising the step of exposing a cell to a small organic compound which interacts with at least one GAG in an amount sufficient for preventing the interactions of the GAG with at least one GAG specific ECAM, wherein HS-GAG and L-selectin are the species.

5. Claim 19 is objected to because the GAG and ECAM should be spelled out in the claim.

6. Claim 26 is objected to because "cytokines" are not effector cell adhesion molecules (ECAM).

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 19-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite "small organic compound" as part of the invention.

However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature that provides the recited function of a small organic compunds. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant

was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

The specification page 37, Table 1 and Table 2 discloses the compounds 1-29. However, neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. The specification provides no structural description of small organic compound; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed small organic compounds looks like. The specification's disclosure is inadequate to describe the claimed genus of small organic compounds.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e1) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

35 U.S.C. § 102(e), as revised by the AIPA and H.R. 2215, applies to all qualifying references, except when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. For such patents, the prior art date is determined under 35 U.S.C. § 102(e) as it existed prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

10. Claims 19-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Peter et al Circulation. (1999 Oct 5;100(14):1533-9), as is evidenced by Yanaka's Letter to the editor (Circulation. 2000;102:e169).

Peter et al article teaches that heparin (small organic compound) inhibits ligand (GAG) binding to the leukocyte integrin Mac-1 (CD11b/CD18) (GAG specific ECAM). Peter et al teach that leukocytes adhere on immobilized heparin mediated by the integrin Mac-1 (CD11b/CD18, αMβ2, or CR3). Because inhibition of this versatile adhesion molecule could explain various aspects of the beneficial clinical effects of heparin, we evaluated whether soluble heparin modulates Mac-1 function in vitro and in vivo. Adhesion of the monocytic cell line THP-1 and of peripheral monocytes and granulocytes to immobilized ICAM-1 was impaired by unfractionated heparin, to the same extent as with inhibition of Mac-1 by monoclonal antibodies such as c7E3. Low-molecular-weight heparin also inhibits binding of fibrinogen to Mac-1. Additionally, flow cytometry of whole blood preparations of patients treated with unfractionated heparin revealed an inhibitory effect of heparin on the binding of fibrinogen to Mac-1 that correlates to the extent of prolongation of the activated partial thromboplastin time. Peter et al concluded that a pharmacologically relevant property of heparin that may contribute to its benefits in clinical use. The binding of heparin to Mac-1 and the resulting inhibition in binding of Mac-1 ligands may directly modulate coagulation, inflammation, and cell proliferation (see abstract in particular). While Peter et al reference is silence with respect to "selectin", Peter et al in response to Yanaka et al letter to the editor (Circulation. 2000;102:e169) agree that the inhibition of P- and L-selectin by heparin can participate in the modulation of cell adhesion by heparin. Peter et al evidentiary references teach that two major adhesion steps of the cascade of leukocyte adhesion, the initial rolling that is mediated by selectins and the buildup of a firm adhesion that is mediated by integrins such as Mac-1, can be inhibited by heparin (see letter to editor and response in particular).

The reference teachings anticipate the claimed invention.

11. Claims 19-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Yanaka et al (Circulation. 2000;102:e169).

Yanaka et al teach that heparin (small organic molecule) inhibits leukocyte adhesion by antagonizing the function of selectins. They evaluated the efficacy of sulfated polysaccharides onleukocyte accumulation in the infracted brain and found that the administration of these sulfated polysaccharides led to reduced leukocyte accumulation. The potency was correlated with the molecule's degree of sulfation. Yanaka et al teach that leukocyte recruitment was due to an interaction between leukocyte selectins (GAG specific ECAM) and carbohydrate ligands (GAG), such as the sulfated polysaccharide side chains of proteoglycans on the endothelia cell surface. Yanaka et al concluded that in addition to integrin Mac-1, selectins also play an important role in the cell adhesion process and this promiscuous binding of heparin may modulate inflammation and cell proliferation.

The reference teachings anticipate the claimed invention.

12. Claims 19-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Haugen et al (J Neurosci. 1992 Jul;12(7):2597-608).

Haugen et al teach that a cell-surface heparan sulfate proteoglycan (GAG) mediates neural cell adhesion and spreading (migration) on a defined sequence from the C-terminal cell and heparin binding domain of fibronectin, FN-C/H II (ECAM). Haugen et al teach that FN-C/H II is a heparin binding synthetic peptide from the C-terminal cell and heparin binding domain of fibronectin (FN) that mediates neuronal cell adhesion, spreading, and neurite outgrowth. Cellular interactions with FN-C/H II are inhibited by soluble heparin, suggesting that a cell-surface proteoglycan may mediate interactions with FN-C/H II. To test this hypothesis further, heparan sulfate (HS) or chondroitin sulfate (CS) was removed from the cell surface by enzyme treatment. Heparitinase but not chondroitinase treatment of cells inhibited rat B104 neuroblastoma cell adhesion and spreading on FN-C/H II. Additionally, heparitinase treatment decreased the spreading of cells on the 33/66 kDa fragments containing the C-terminal heparin binding domain of FN. Furthermore, antibodies generated against a mouse melanoma HS proteoglycan (HSPG) inhibited B104 cell adhesion to FN-C/H II and the 33/66 kDa FN fragments. 35S-HSPG isolated from B104 cells directly bound to FN-C/H II both in solid phase assays and by affinity chromatography, but failed to bind to a control peptide from this region, CS1. The binding of 35S-HSPG was predominantly mediated by the HS and not the core protein of the HSPG (see abstract in particular).

The reference teachings anticipate the claimed invention.

12. Claims 19-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Diamond et al, 1995 (of record).

Diamond et al teach that inhibition studies with mAbs and chemically modified forms of heparin (small organic compounds) suggest the I-domain as a recognition site on Mac-1 (GAG specific ECAM) for heparin (GAG), and suggest that either N- or O-sulfation is sufficient for heparin to bind efficiently to Mac-1. Under conditions of continuous flow in which heparins and E-selectin are cosubstrates, neutrophils tether to E-selectin and form firm adhesions through a Mac-l-heparin interaction (see abstract). Further, Diamond et al evaluated the interaction more quantitatively, they tested soluble heparin (small organic molecule) for its ability to inhibit Mac-I (GAG specific ECAM) dependent neutrophil adhesion to immobilized heparin (GAG) (Fig. 5). Preincubation of neutrophils with soluble heparin dose dependently inhibited adhesion to heparin (see page 1476, 2nd col., 1st full ¶).

The reference teachings anticipate the claimed invention.

13. Claims 19-27 are rejected under 35 U.S.C. 102(e) as being anticipated by US. Pat. No. 6,596,705.

The '705 patent teaches and claims methods of inhibiting L-selectin and P-selectin (GAG specific ECAM) mediated binding in a subject by administering heparin (a small organic compound) to the subject. In addition, the invention provides methods of treating a subject

having a pathology characterized, at least in part, by abnormal L-selectin or P-selectin mediated binding by administering heparin to the subject in an amount that results in attaining a concentration of less than about 0.2-0.4 units heparin per ml of plasma in the subject, wherein the pathology is selected from the group consisting of ischemia, reperfusion injury, acute inflammation, chronic inflammation, and cancer metastasis (see patented all claims). The `705 patent further teaches that the binding of heparin sulfate glycosaminoglycan chains (HS-GAG) by L-selectin, is calcium-dependent (FIG. 2A). Also, the binding of heparin sulfate glycosaminoglycan chains (HS-GAG) by P-selectin is not calcium-dependent (Fig. 2B). HS-GAG chains were applied either to an L-selectin or P-selectin column in the presence of 5 mM calcium (solid triangles) or of magnesium/EGTA (open circles). The elution profiles were obtained using 5 mM EDTA buffer for L-selectin and 20 mM EDTA buffer for P-selectin (col., 3, lines 7-15 and col., 11, lines 3-25). The `705 patent teaches that selectin adhesion is involved in disorders such as pathologic reperfusion injury, inflammatory disorders and autoimmune disorders (col., 1 lines 36-38). Further, the patent teaches that undesirable immune responses in which the homing or adhesion of leukocytes, neutrophils, macrophages, eosinophils or other immune cells mediated by the interaction of L-selectin with endothelial cell ligands, can be inhibited by administering heparin to the subject according to a method of the invention (col., 19, lines 25-32).

The reference teachings anticipate the claimed invention.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 19-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15-28 of U.S. Patent No. 7,365,080. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the patented claims claiming a method of inhibiting GAG-L-selecting interactions, comprising the step of administering a mall organic compound.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 3, 2008

/Maher M. Haddad/
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